EXHIBIT 2

Knee Surg Sports Traumatol Arthrosc (2011) 19:899–903
DOI 10.1007/s00167-010-1218-x

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Three- to six-year follow-up results after high-flexion total knee arthroplasty: can we allow passive deep knee bending?

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Received: 7 December 2009 / Accepted: 6 July 2010 / Published online: 29 July 2010

Abstract
Purpose We evaluated 3- to 6-year clinical and radiological follow-up results after NexGen® LPS-flex total knee arthroplasty (TKA).
Methods A retrospective evaluation was undertaken of 218 knees in 166 patients (22 males, 144 females) who were followed up for more than 3 years after TKA. Evaluations included preoperative and postoperative range of motion (ROM) measurement, Knee Society (KS) Score, tibiofemoral angle and assessment of postoperative complications.
Results TKA resulted in a significant ROM increase from a mean flexion contracture of 9° (range 0°–20°) and further flexion of 117° (range 80°–155°) to a mean flexion contracture of 2° (range 0°–10°) and a further flexion of 131° (range 95°–155°). KS knee and function scores significantly improved from 52 and 38 before surgery to 87 and 82 after surgery, respectively. The tibiofemoral angle significantly improved from varus 5.7° to valgus 5.4°. Progressive radiolucent lines around the femoral component on radiographs were observed in 30 knees (13.8%, 27 patients), and more of those knees, could squat than non-radiolucent knees (76.7 vs. 20.2%; $P < 0.05$). Seven knees (3.2%, 6 patients) were revised at a mean 49 months after the index operation.
Conclusions While NexGen® LPS-flex TKA satisfactorily improved ROM, it was associated with a relatively high incidence of early loosening of the femoral components. This might be associated with passive-maximal flexion activity, such as squatting or kneeling. The clinical relevance of this study is that squatting or kneeling, common activity in Asian, may not be allowed after NexGen® LPS-flex TKA.

Keywords Total knee arthroplasty · Nexgen LPS-flex · Early loosening · Squatting · Kneeling

Introduction

It is generally agreed that at least 90° of knee flexion is necessary for usual daily activities [9]. Total knee arthroplasty (TKA) employing modern prostheses and surgical techniques can allow flexion of the knee of up to 110°–120° [2, 14]. However, in some non-Western countries, such as Korea and Japan, squatting, kneeling, and sitting on the floor are common daily activities. These positions require knee flexion of 111°–165° [16].

The NexGen® legacy posterior stabilized (LPS)-flex total knee system (Zimmer, Warsaw, IN) is designed to provide 150° of flexion following TKA. With this new system (modified from the NexGen® LPS prosthesis), the posterior femoral condyles are elongated by 2 mm to increase the articulation curvature during deep flexion, and the anterior margin of the tibial articular component is removed to avoid interference with the patellar tendon during deep flexion. The modified post-cam mechanism also allows a greater jump distance and prevents dislocation at deep flexion angles.

A recent report found a high incidence of loosening of the femoral component related to the deep flexion provided by TKA [7]. It was hypothesized that the findings from our cases may be similar to the findings of that study. Thus, we retrospectively evaluated the clinical and radiographical

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results of patients who received TKA using the NexGen® LPS-flex system, at a minimum of 3 years after surgery, and documented the complications, including early loosening of femoral components.

Materials and methods

From October 2001 to February 2005, 259 consecutive primary TKAs were performed in 192 patients using the NexGen® LPS-flex system. A retrospective evaluation was undertaken of 218 knees in 166 patients (22 males, 144 females), who were followed up for more than 3 years after TKA. The average patient age was 64.2 years at the time of surgery. The mean follow-up period was 51 months (range 36–73 months). The primary diagnosis was osteoarthritis in 208 knees (95.4%), including one knee with post-traumatic osteoarthritis, rheumatoid arthritis in 4 knees (1.8%), and osteonecrosis in 6 knees (2.8%). Patients with previous arthroplasty, osteotomy, severe extra-articular deformity and open reduction and internal fixation for fractures about the knee were excluded.

Surgical methods and postoperative rehabilitation

All surgeries were performed by the first senior author using a standard medial parapatellar arthrotomy. Medial soft tissue release was performed by elevating a subperiosteal sleeve from the proximal anteromedial tibia to a posteromedial aspect. The anterior and posterior cruciate ligaments were resected. The intramedullary method was used for distal femoral osteotomies, while the extramedullary method was used for the proximal tibia. The femoral component was implanted with 3° of external rotation to the posterior condylar axis. The aim was to make a tibial cut with a posterior slope of $\sim 7°$. Ligament balancing was performed until the knee was stable in flexion and extension, according to valgus and varus stress tests. All implants were cemented using Simplex P (Howmedica, Rutherford, NJ). The cement was applied to the whole inner surface of the femoral implant including the posterior condylar portion.

Patients were preoperatively educated with regard to quadriceps strengthening and straight leg raising exercises, and these were performed immediately after the operation. The continuous passive knee motion exercise was initiated 1 day after the operation. Weight bearing with a cane or walker was performed as soon as possible after surgery.

Clinical and radiological evaluations

Clinical evaluations included determination of preoperative and postoperative range of motion (ROM), Knee Society (KS) knee and function scores, and postoperative complications. Flexion of the knee joint was measured using a standard clinical goniometer with the patient in a supine position. Maximal flexion was determined as the point where the patient first felt slight pain upon knee bending. Radiological evaluations included analysis of the tibiofemoral angle, the position of implants assessed using the method of the American Knee Society Roentgenographic Evaluation in the standing anteroposterior (AP) view, and a lateral view of 30° knee flexion at the final follow-up. Fluoroscopy was used to check the true AP and lateral views. The position and alignment of implants was measured in the AP and lateral views, with angle α (valgus angle of the femoral component) and angle β (varus angle of tibial component) measured in the former, and angle γ (position of the femoral component; flexion angle) and angle δ (position of the tibial component; posterior slope) in the latter. All parameters on radiographs were measured to two decimal places using a picture archiving communication system (PACS; Pi view STAR software, Infinitt, Seoul, Korea), and calculated results were expressed to one decimal place.

Statistical analysis

Paired *t*-tests were used to compare clinical outcomes and changes in the tibiofemoral angle before and after surgery, using commercially available software (SPSS, Chicago, Illinois, USA). P values < 0.05 were considered statistically significant.

Results

ROM significantly increased at the final follow-up (Table 1; $P < 0.05$). The mean further flexion angle at the final follow-up was less than 120° in 21 knees (9.6%), 120°–140° in 133 knees (61.0%), and more than 140° in 64 knees (29.4%). A total of 191 knees (87.6%) allowed patients to sit cross-legged and 61 knees (27.9%) allowed patients to squat. Also, the KS knee and function scores were significantly improved at the final follow-up (Table 1; $P < 0.05$).

Table 1 Clinical assessment by average range of motion and knee society scores

	Preoperative	Postoperative
Range of motion	FC 9° FF 117°	FC 2° FF 131°
Knee score	52 (34–66)	87 (73–97)
Function score	38 (25–45)	82 (60–80)

FC flexion contracture, *FF* further flexion

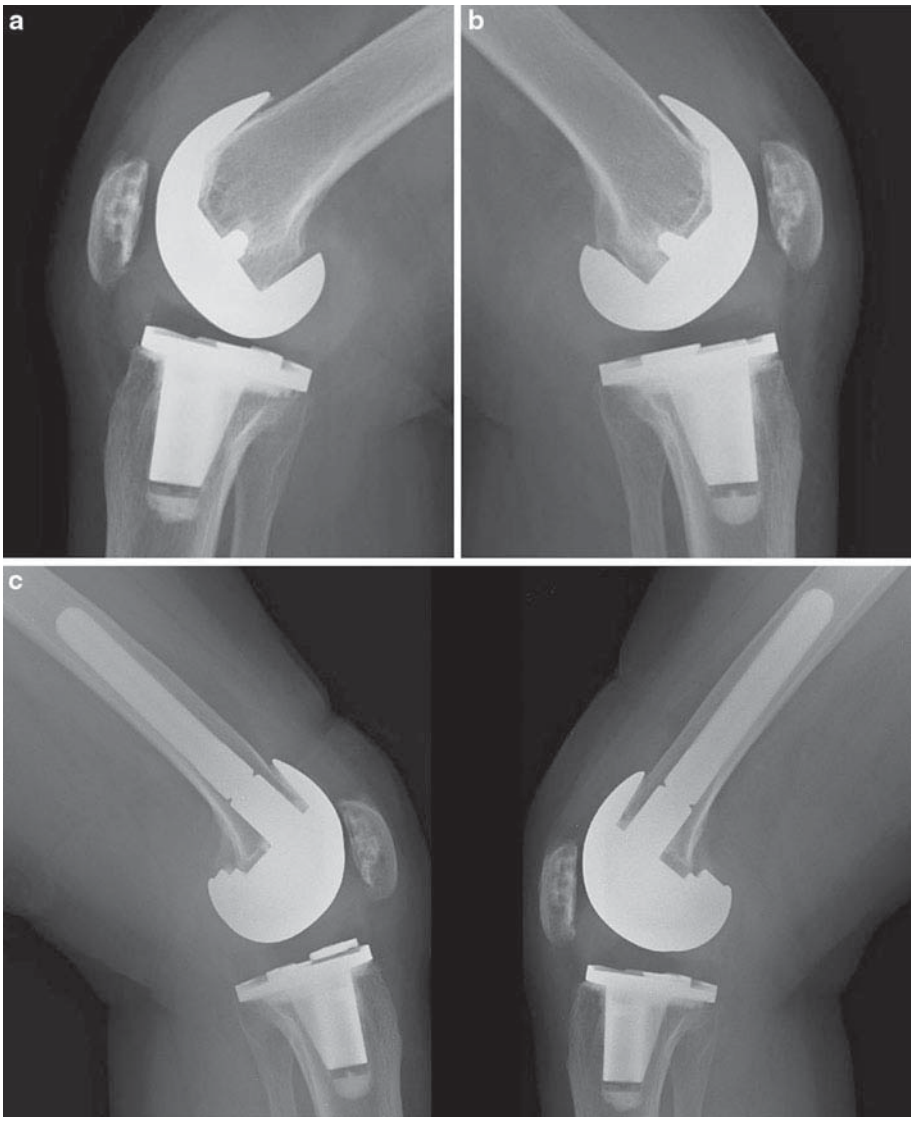

Fig. 1 Radiographs showing early failure of the femoral component. Lateral views of **a** right and **b** left knee 3 years after surgery, showing *radiolucent lines* around the anterior and posterior flanges. **c** Revision surgeries using a stemmed femoral component and a structural allograft were performed on both knees because of early loosening of the femoral component

The tibiofemoral angle significantly improved, with a preoperative varus of 5.7° ± 4.3° to an immediate postoperative valgus of 5.4° ± 2.2° ($P < 0.05$). The postoperative mean of angle α was 96.2° ± 2.9°, of angle β 88.6° ± 1.9°, of angle γ 2.5° ± 1.2°, and of angle δ 84.7° ± 3.1°.

There were progressive radiolucent lines around the femoral component on the radiographs of 30 knees (13.8%, 27 patients), instability in 2 knees (0.9%), periprosthetic fracture in 2 knees (0.9%), and failure of the extensor mechanism in 1 knee (0.5%).

Early progressive radiolucent lines around the femoral component were found at a mean period of 24 months (range 6–76 months) after surgery. In all patients, only femoral components were involved. Radiolucent lines were detected beneath the anterior flanges or the posterior condyle of the femoral component on lateral radiographs. The mean ROM of these patients was 142° (range 95°–155°). Among these 30 knees, 23 knees allowed patients to squat, 5 knees could flex over 130°, 1 knee could flex up to 115°, and 1 knee could flex up to 95°. Of those, 7 knees (3.2%, 6 patients) were revised at a mean 49 months (range 27–76 months) after initial operation (Fig. 1) due to pain or swelling. Upon re-operation, all femoral implants were easily removed by hand and were completely dissociated from the cement mantles (Fig. 2).

In comparison between knees which showed progressive radiolucent lines (radiolucent group, 30 knees) and knees which did not show such lines (non-radiolucent group, 188 knees), the mean ROM was 142° in the radiolucent group and 128° in non-radiolucent group, and this difference was statistically significant ($P < 0.05$). In the radiolucent group, 23 of the 30 knees (76.7%) could squat, compared with 38 of 188 knees (20.2%) in the non-radiolucent group. This difference was also statistically significant ($P < 0.05$). In the two cases with poor postoperative ROM, preoperative ROM was less than 90°.

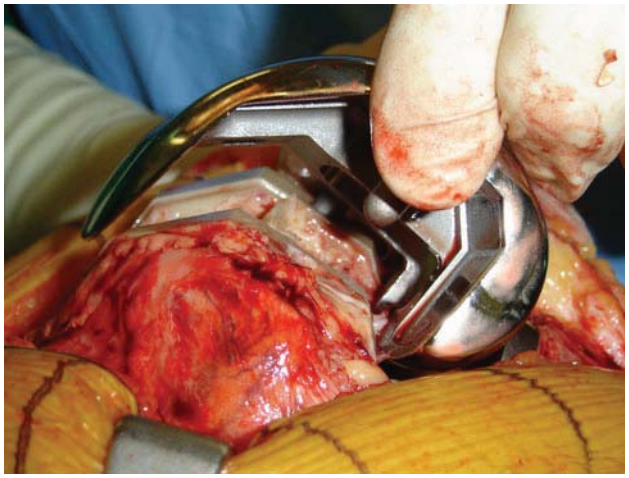

Fig. 2 Intraoperative finding of removed femoral component, showing dissociation of the cement-implant interface

In two instability case, the patients were treated by use of thicker polyethylene. One intraoperative medial condylar fracture of the femur and one traumatic avulsion fracture of the tibial tuberosity were treated by open reduction and internal fixation, resulted in a good outcome. In one patient with an extensor mechanism rupture, the patient underwent several operations in our hospital and other hospitals necessitated by repeated re-rupture. None of these surgeries was successful, and the patient was ultimately lost to follow-up.

Discussion

The most important finding of the present study was that while NexGen® LPS-flex TKA outcomes after a minimum 3-year follow-up were satisfactory in terms of knee ROM, it was also associated with a relatively high incidence of early loosening of the femoral components. Patient satisfaction with TKA depends on relief from pain and restoration or improvement in ROM [1, 4, 5, 12]. Ritter and Campbell [20] reported that the amount of knee flexion significantly influenced the ability of patients to climb stairs and walk. In the Far and Middle East, the inability to flex beyond 120° may prevent patients from participating in normal cultural activities that involve kneeling and squatting [16].

The NexGen® LPS-flex total knee system was designed to provide 150° of flexion following TKA [15]. Huang et al. [8] reported that patients given high-flex TKA had an average knee flexion of 138° and that 80% of such patients were able to squat after a minimum of 2 years of follow-up, with no complications such as osteolysis, infection, or loosening. Bin et al. [3] reported that patients given high-flex TKA had an average maximal flexion of 129.8° (significantly higher than the 124.3° in patients given conventional LPS) and experienced no complications. Using the same implants, Kim et al. [10] reported that the mean maximum flexion was 135° after a minimum of 3 years of follow-up. In our present study, the mean maximal flexion was 131° after a minimum of 3 years of follow-up.

Kim et al. [11] reported that, after a minimum follow-up time of 2 years, there were no significant differences between NexGen® LPS and NexGen® LPS-flex with regard to ROM, clinical parameters, or radiography. Turning to patient expectations, Park et al. [19] found that Korean patients who received TKA rated high-flexion activities as the most difficult, but the patients did not consider these activities to be more important than pain relief and the ability to participate in routine daily activities.

However, there have been several reports on the risk of high knee flexion [6]. Deep knee flexion activities generate larger net quadriceps moments (6.9–13.5% of body weight) and net posterior forces (58.3–67.8% of body weight) than do routine ambulatory activities. Moreover, peak net moments and net posterior forces are generated between 90° and 150° of knee flexion. These larger moments and forces mean that high stress is associated with high-flexion angles [17]. Also, in deep flexion, large stresses can develop, and these can cause cartilage damage in the normal knee [21].

Nakayama et al. [18] suggested that very high contact stress was inevitable at the post-cam mechanism considering the current design of posterior stabilized TKA components. These authors also recommended against deep knee flexion and deep bending of the knee in patients who had undergone posterior stabilized TKA. Han et al. [7] reported that aseptic loosening of the femoral component occurred in 27 of 71 knees (38%) following NexGen® LPS-flex TKA at a mean follow-up time of 32 months (range 30–48 months), and that 15 of 71 knees (21%) required revision surgery after a mean period of 23 months. These authors concluded that the NexGen® LPS-flex implants allowed a high degree of flexion, but their use was also associated with a high rate of early loosening of the femoral component, attributable to weight bearing at maximal flexion. The present procedure differed from that used in the Kim et al.'s [11] study in terms of approach (midvastus vs. subvastus) and tibial posterior slope (0° vs. 7°). However, that study did not report on exact cementing techniques, the proportion of patients who could undertake weight-bearing high-flexion activities such as squatting or kneeling, and whether those activities were permitted or not. Therefore, it is difficult to identify reasons that may explain the differences in early loosening between the studies. In the

present study, radiography indicated that 30 of 218 knees (13.8%) showed early progressive radiolucent lines around the femoral components. The percentage of knees that could squat was significantly higher in the radiolucent group (76.7%) than that in non-radiolucent group (20.2%). Among these 30 knees, we performed revision surgery on 7 knees (3.2%). A traditional Korean lifestyle involves passive-maximal flexion activities such as squatting and kneeling, especially for farmer. Some patients continued with farming activities after TKA, despite being warned not to do, and this may explain the relatively high rate of early loosening in the present study.

King and Scott [13] reported that loosening of the femoral component following TKA occurred in only 15 of over 1,600 knees. These authors suggested that the loosening might be related to inadequate support of the prosthetic posterior condyle, which may have resulted from inaccurate surgical cuts, poor cementing technique, or deficient bone stock. In the present study, lateral radiographs indicated radiolucent lines beneath the anterior flanges and posterior condyle of the femoral component in 30 knees. In addition, the NexGen® LPS-flex showed the greatest increase in stress at 150° of flexion because of edge loading, and in PS design, very high contact stress is inevitable at the post-cam mechanism during deep bending [18]. Since March 2005, we used the LPS (not LPS-flex) total knee system and forbade patients from squatting or kneeling in their daily activities. Since that time, there have been no cases of early loosening. Thus, it was hypothesized that with passive deep knee bending, excessive compressive force could be applied at the posterior femoral condyle, leading to distal shear and anterior tensile forces, in agreement with the suggestions of King and Scott [13]. Inadequate bony support of the posterior femoral condyle may result in micromotion and early loosening of the femoral component.

The limitations of this study included a relatively short follow-up period, its retrospective nature and the lack of a control group. Given that revision rates can increase over time, long-term outpatient clinic contact is important.

Conclusions

While NexGen® LPS-flex TKA satisfactorily improved knee ROM, it was also associated with a relatively high incidence of early loosening of the femoral components. This adverse effect might be related to passive-maximal flexion activity, such as squatting or kneeling. The clinical relevance of this study is that squatting or kneeling, common activity in Asian, may not be allowed after NexGen® LPS-flex TKA.

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